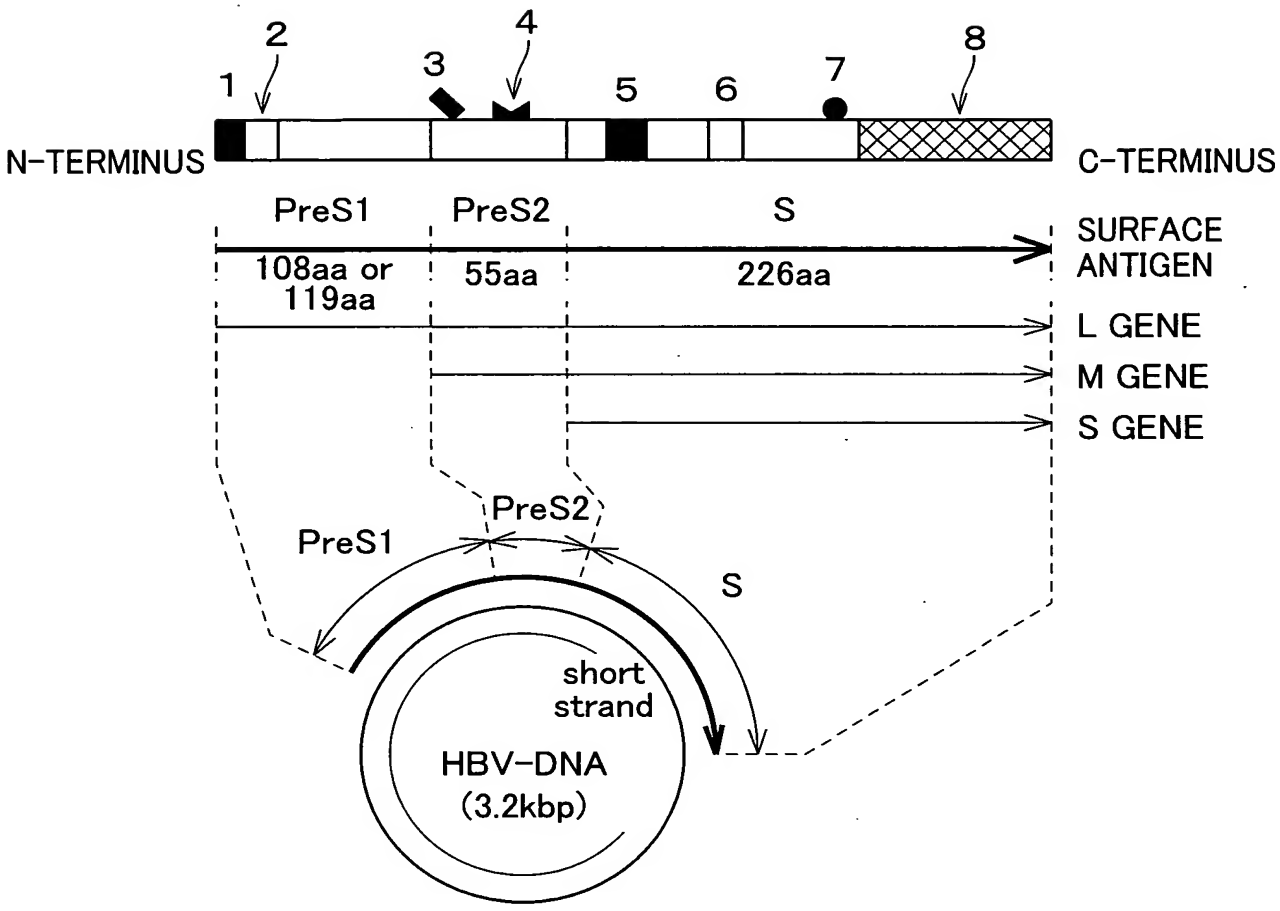
FIG. 1



1 PARTICLE FORMATION SUPPRESSING SITE
2 DIRECT RECEPTOR SPECIFIC TO HUMAN HEPATOCYTE
3 SUGAR CHAIN 1
4 INDIRECT HUMAN HEPATOCYTE SPECIFIC RECEPTOR (POLYMERIZED HUMAN SERUM ALUBUMIN RECEPTOR)
5 TRANSMENBRANE REGION 1
6 TRANSMEMBRANE REGION 2
7 SUGAR CHAIN 2
8 TRANSMEMBRANE REGION 3

FIG. 2

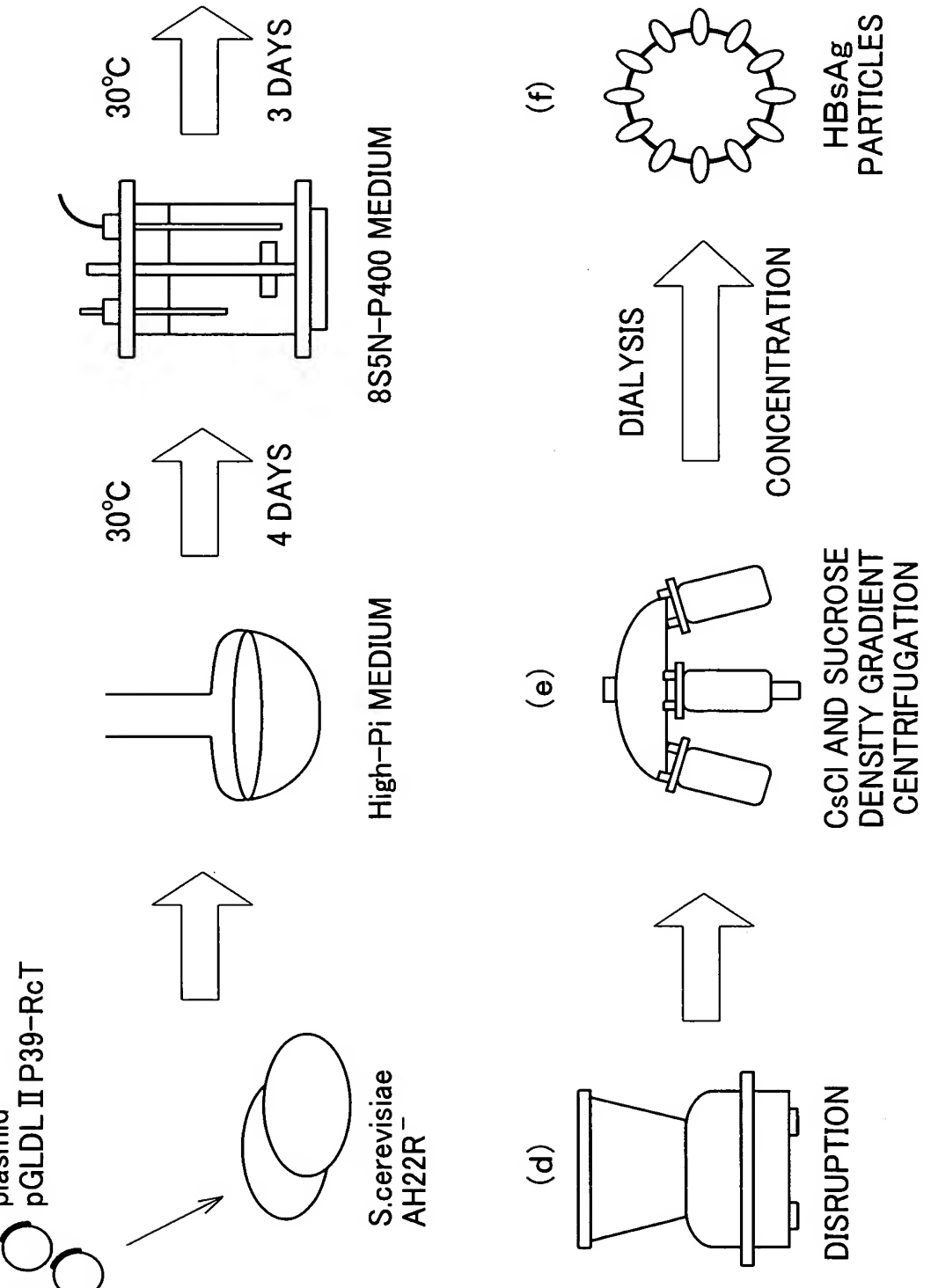

(a)
plasmid
pGLDL II P39-RcT
S.cerevisiae
AH22R⁻
(b)
High-Pi MEDIUM
30°C
4 DAYS
(c)
8S5N-P400 MEDIUM
30°C
3 DAYS
(d)
DISRUPTION
(e)
CsCl AND SUCROSE
DENSITY GRADIENT
CENTRIFUGATION
DIALYSIS
CONCENTRATION
(f)
HBsAg
PARTICLES

FIG. 3

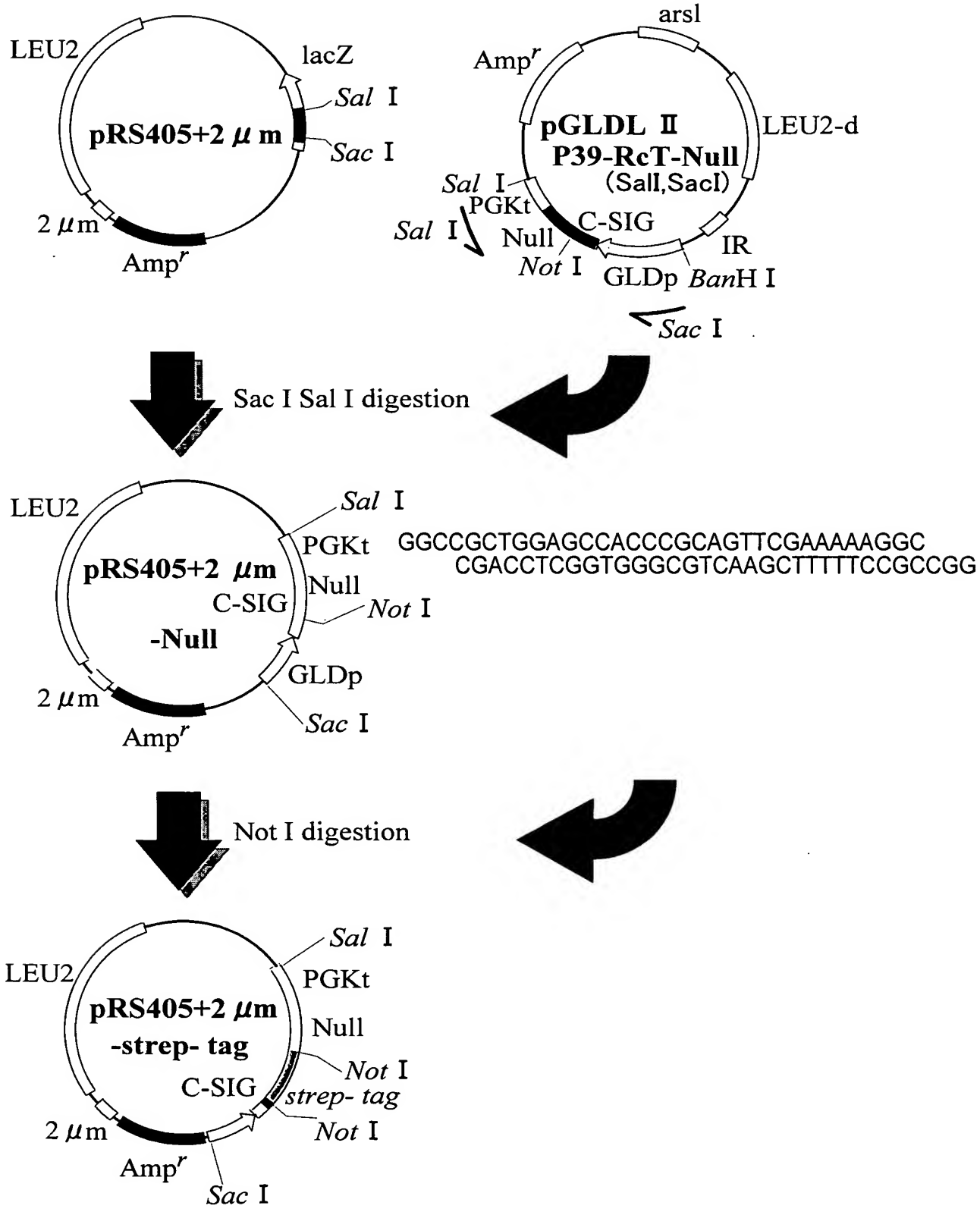

LEU2
lacZ
Sal I
pRS405+2 μ m
Sac I
2 μm
Ampr
arsl
Ampr
pGLDL II
P39-RcT-Null
(SalI,SacI)
LEU2-d
Sal I
PGKt
Sal I
C-SIG
Null
IR
Not I
GLDp
BanH I
Sac I
Sac I Sal I digestion
LEU2
Sal I
PGKt
pRS405+2 μm
Null
C-SIG
Not I
-Null
GLDp
2 μm
Sac I
Ampr
GGCCGCTGGAGCCACCCGCAGTTCGAAAAAGGC
CGACCTCGGTGGGCGTCAAGCTTTTTCCGCCGG
Not I digestion
LEU2
Sal I
PGKt
pRS405+2 μm
Null
-strep- tag
Not I
C-SIG
strep- tag
2 μm
Not I
Ampr
Sac I

FIG. 4

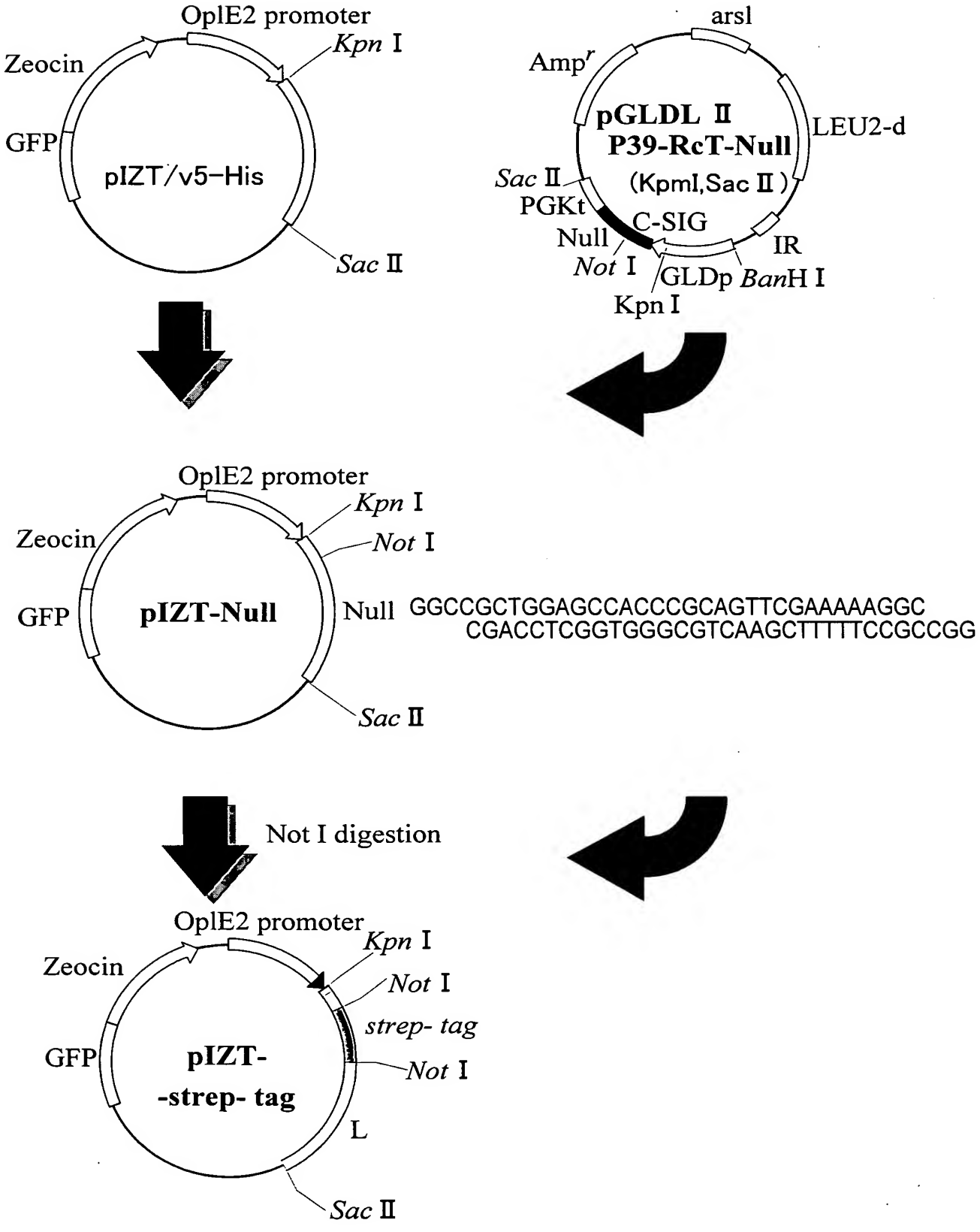

OplE2 promoter
Kpn I
Zeocin
GFP
pIZT/v5-His
Sac II
arsl
Amp^r
pGLDL II
P39-RcT-Null
(KpmI,Sac II)
LEU2-d
Sac II
PGKt
C-SIG
Null
Not I
IR
GLDp
BanH I
Kpn I
OplE2 promoter
Kpn I
Not I
Zeocin
GFP
pIZT-Null
Null
GGCCGCTGGAGCCACCCGCAGTTCGAAAAAGGC
CGACCTCGGTGGGCGTCAAGCTTTTTCCGCCGG
Sac II
Not I digestion
OplE2 promoter
Kpn I
Not I
Zeocin
strep- tag
GFP
pIZT-
-strep- tag
Not I
L
Sac II

FIG. 5

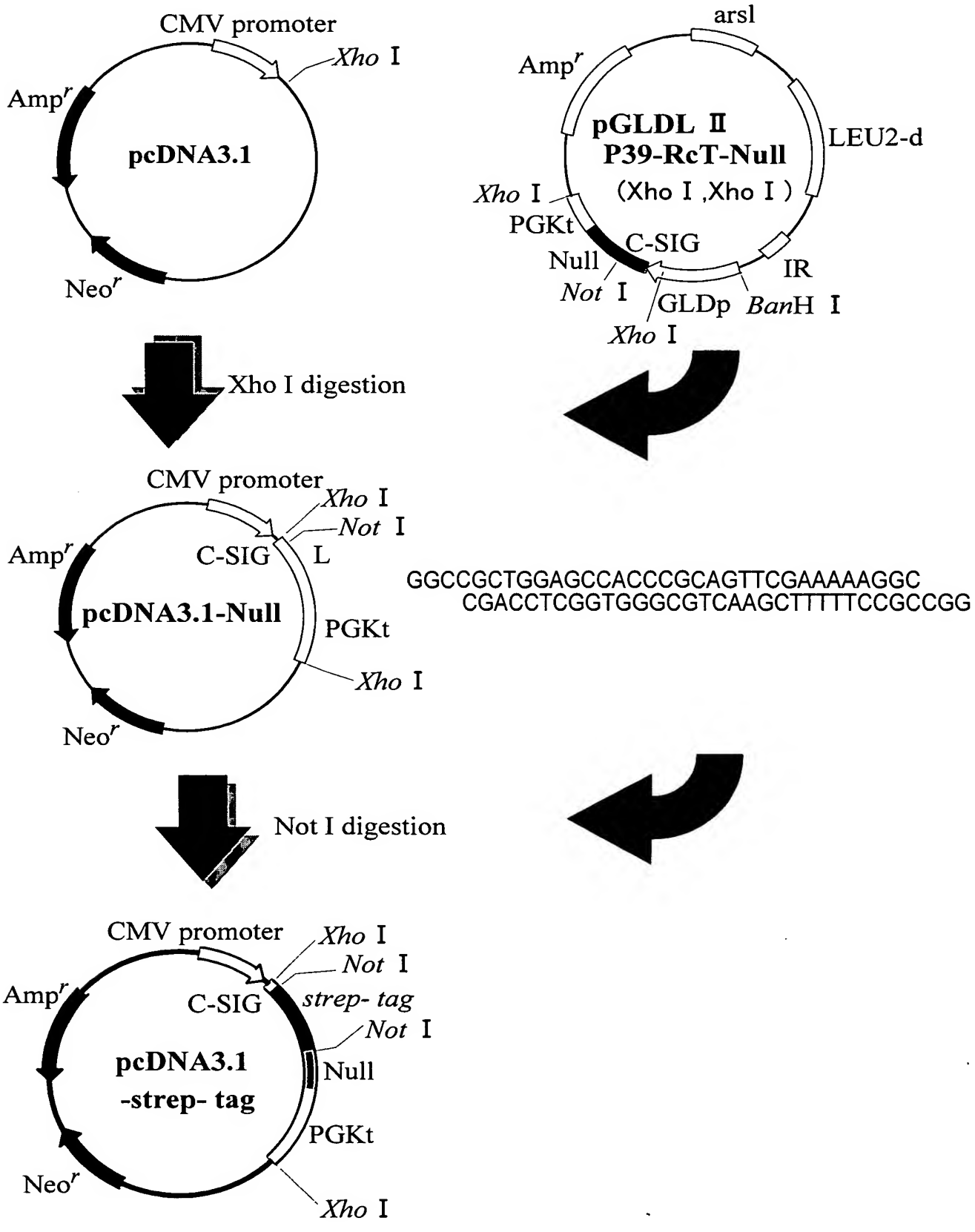

CMV promoter
Xho I
Amp^r
pcDNA3.1
Neo^r
Xho I digestion
CMV promoter
Xho I
Not I
Amp^r
C-SIG
L
pcDNA3.1-Null
PGKt
Xho I
Neo^r
Not I digestion
CMV promoter
Xho I
Not I
Amp^r
C-SIG
strep- tag
Not I
pcDNA3.1
-strep- tag
Null
PGKt
Neo^r
Xho I
arsl
Amp^r
pGLDL II
P39-RcT-Null
(Xho I ,Xho I)
LEU2-d
Xho I
PGKt
C-SIG
Null
IR
Not I
GLDp
BanH I
Xho I
GGCCGCTGGAGCCACCCGCAGTTCGAAAAAGGC
CGACCTCGGTGGGCGTCAAGCTTTTTCCGCCGG

FIG. 6

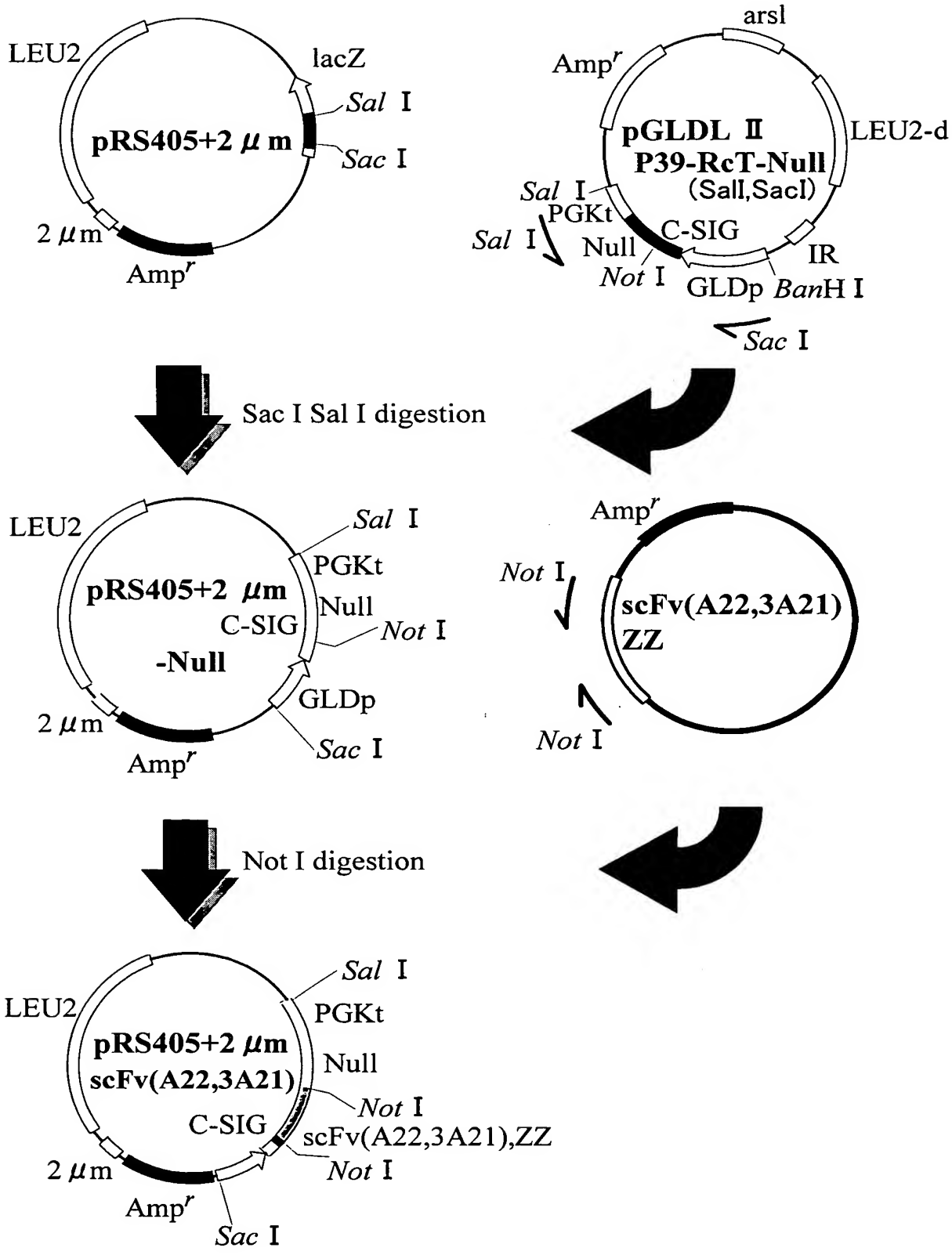

LEU2
lacZ
Sal I
pRS405+2 μm
Sac I
2 μm
Ampr
arsl
Ampr
pGLDL II
P39-RcT-Null
(SalI,SacI)
LEU2-d
Sal I
PGKt
Sal I
Null
C-SIG
IR
Not I
GLDp
BanH I
Sac I
Sac I Sal I digestion
LEU2
Sal I
PGKt
pRS405+2 μm
Null
C-SIG
Not I
-Null
GLDp
2 μm
Sac I
Ampr
Ampr
Not I
scFv(A22,3A21)
ZZ
Not I
Not I digestion
LEU2
Sal I
PGKt
pRS405+2 μm
scFv(A22,3A21)
Null
Not I
C-SIG
scFv(A22,3A21),ZZ
2 μm
Not I
Ampr
Sac I

FIG. 7

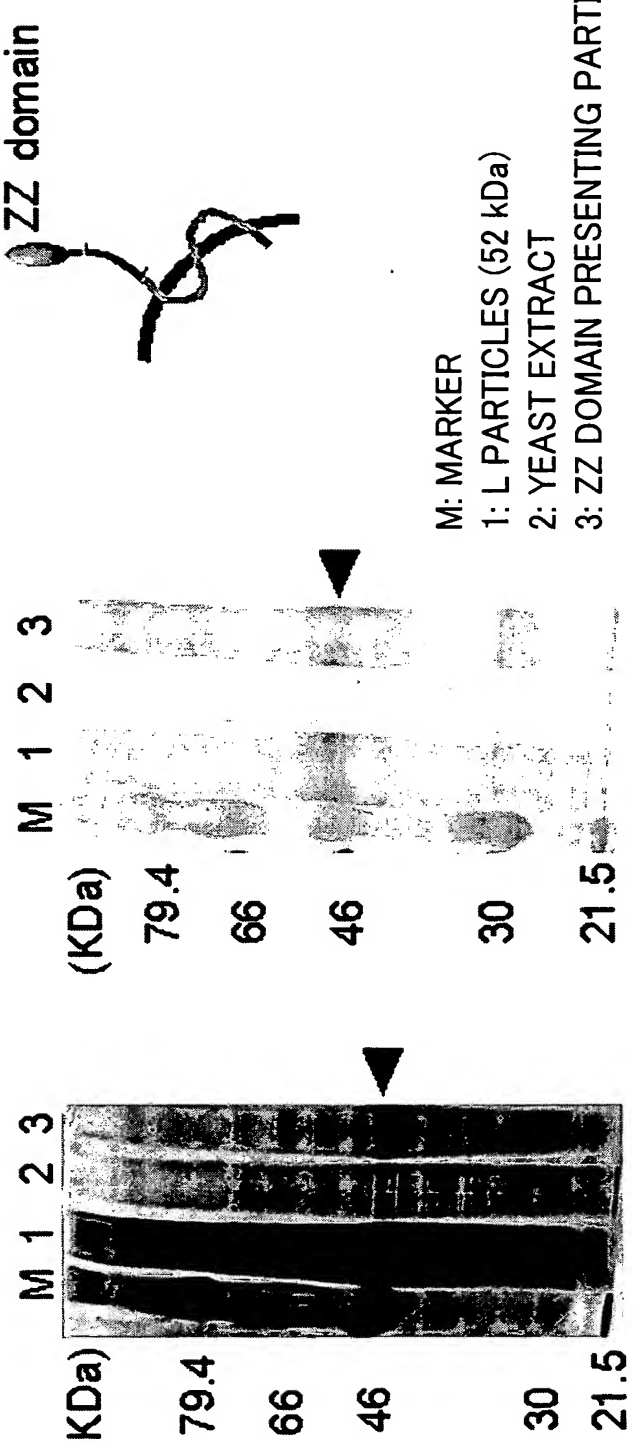

ZZ domain
M: MARKER
1: L PARTICLES (52 kDa)
2: YEAST EXTRACT
3: ZZ DOMAIN PRESENTING PARTICLES (56 kDa)
M 1 2 3
(KDa)
79.4
66
46
30
21.5
M 1 2 3
(KDa)
79.4
66
46
30
21.5

FIG. 8

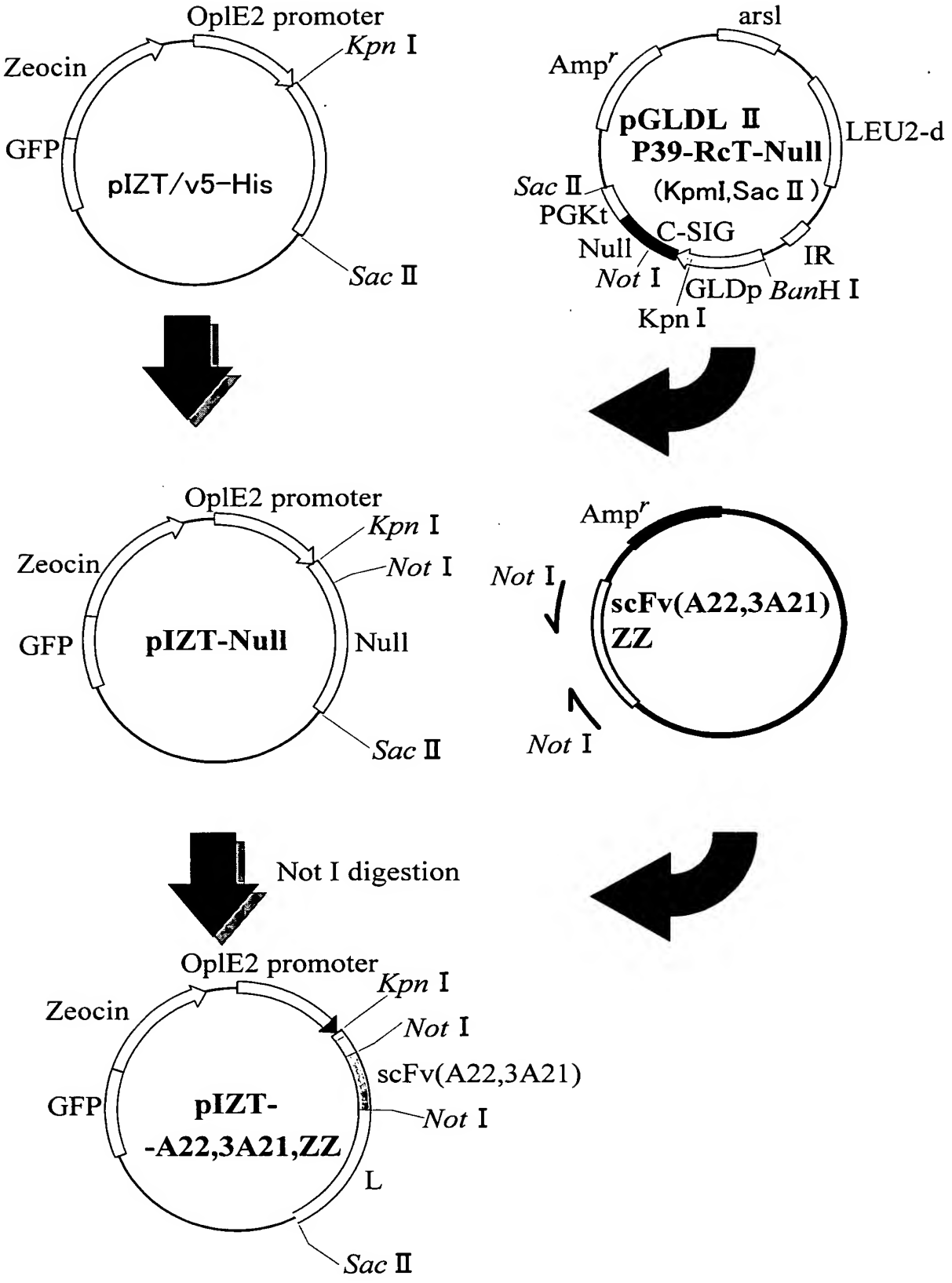

OplE2 promoter
Kpn I
Zeocin
GFP
pIZT/v5-His
Sac II
arsl
Amp^r
pGLDL II
P39-RcT-Null
(KpmI,Sac II)
LEU2-d
Sac II
PGKt
C-SIG
Null
Not I
IR
GLDp
BanH I
Kpn I
OplE2 promoter
Kpn I
Not I
Zeocin
GFP
pIZT-Null
Null
Sac II
Amp^r
Not I
scFv(A22,3A21)
ZZ
Not I
Not I digestion
OplE2 promoter
Kpn I
Not I
Zeocin
scFv(A22,3A21)
GFP
pIZT-
-A22,3A21,ZZ
Not I
L
Sac II

FIG. 9

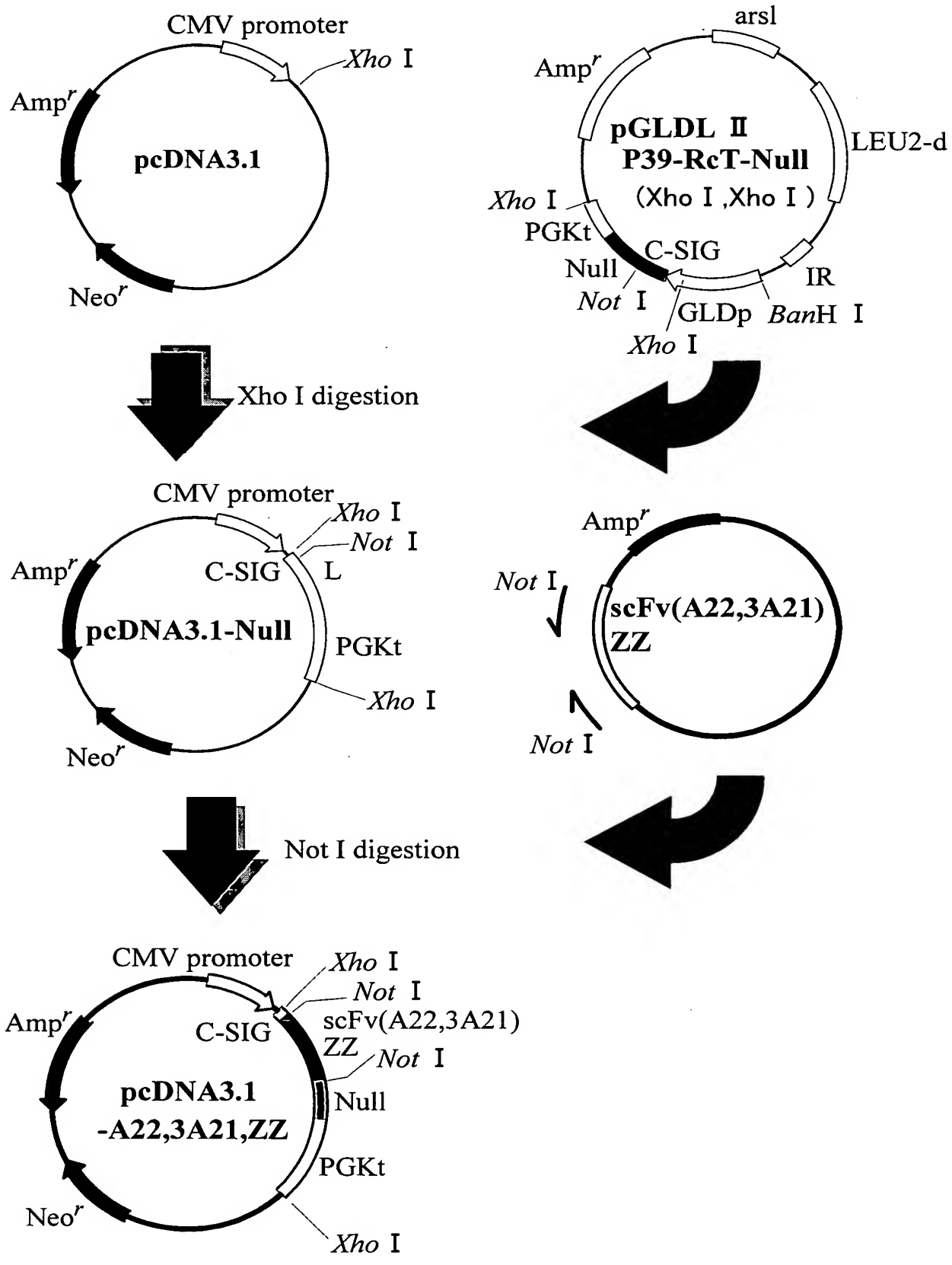

CMV promoter
Xho I
Amp^r
pcDNA3.1
Neo^r
Xho I digestion
arsl
Amp^r
pGLDL II
P39-RcT-Null
(Xho I ,Xho I)
LEU2-d
Xho I
PGKt
C-SIG
Null
Not I
IR
GLDp
BanH I
Xho I
CMV promoter
Xho I
Not I
Amp^r
C-SIG
L
pcDNA3.1-Null
PGKt
Xho I
Neo^r
Amp^r
Not I
scFv(A22,3A21)
ZZ
Not I
Not I digestion
CMV promoter
Xho I
Not I
Amp^r
C-SIG
scFv(A22,3A21)
ZZ
Not I
pcDNA3.1
-A22,3A21,ZZ
Null
PGKt
Neo^r
Xho I

FIG. 10

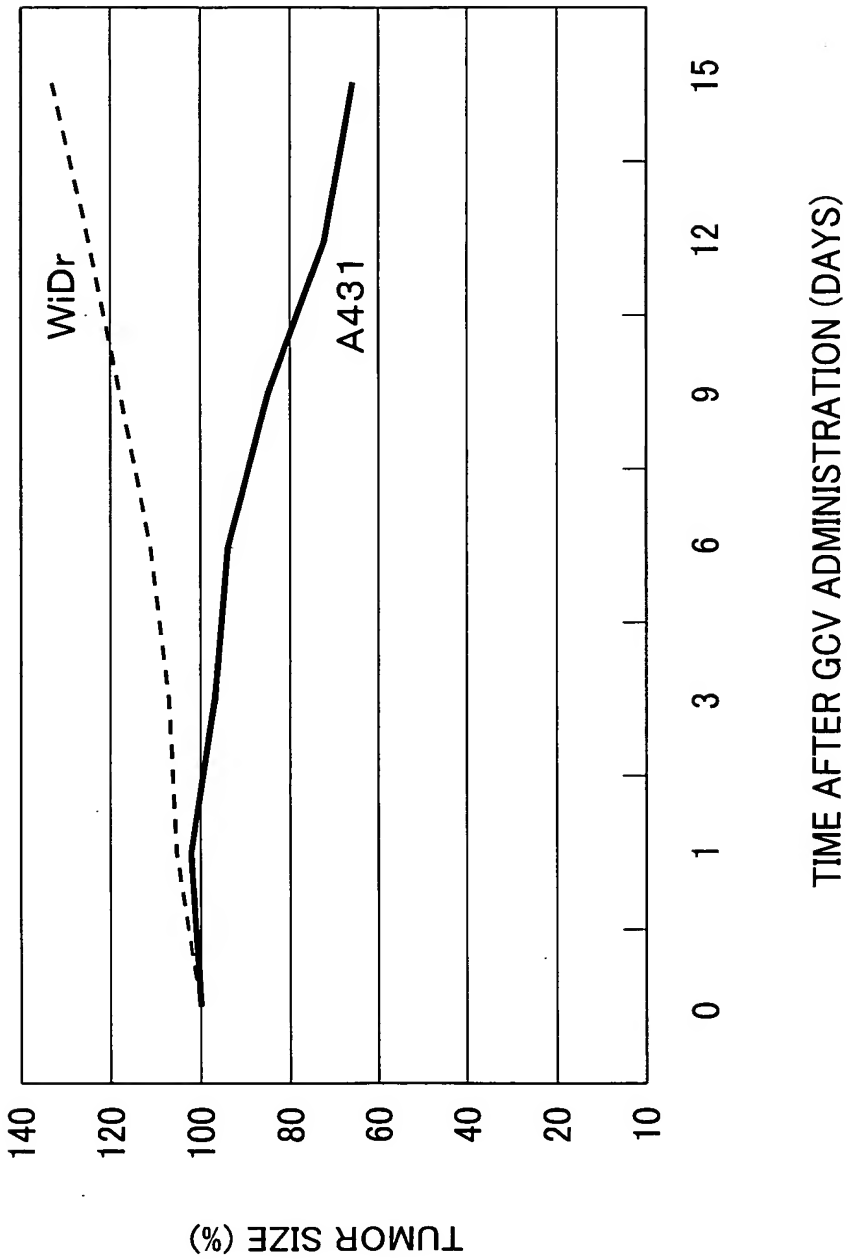

TUMOR SIZE (%)
140
120
100
80
60
40
20
10
WiDr
A431
0
1
3
6
9
12
15
TIME AFTER GCV ADMINISTRATION (DAYS)

FIG. 11

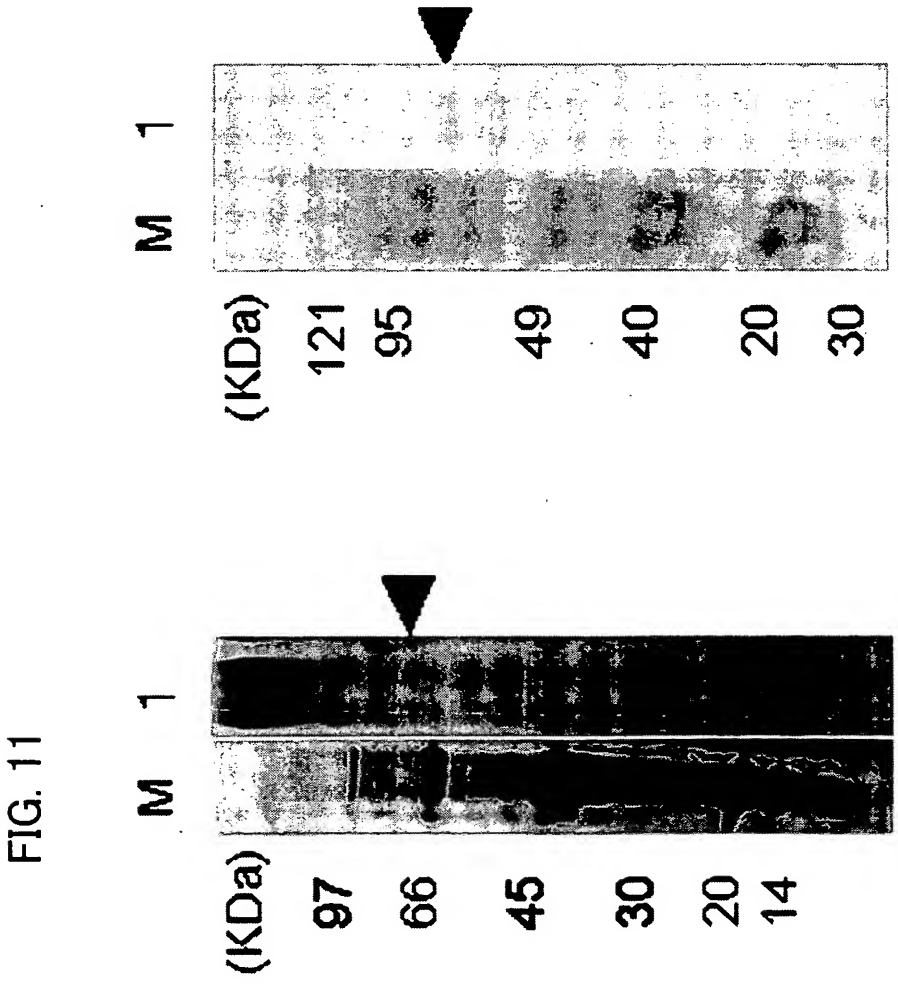

M
1
(KDa)
97
66
45
30
20
14
M
1
(KDa)
121
95
49
40
20
30
scFv(A22)
M: MARKER
1: A22 PRESENTING PARTICLES (76 kDa)

FIG. 12

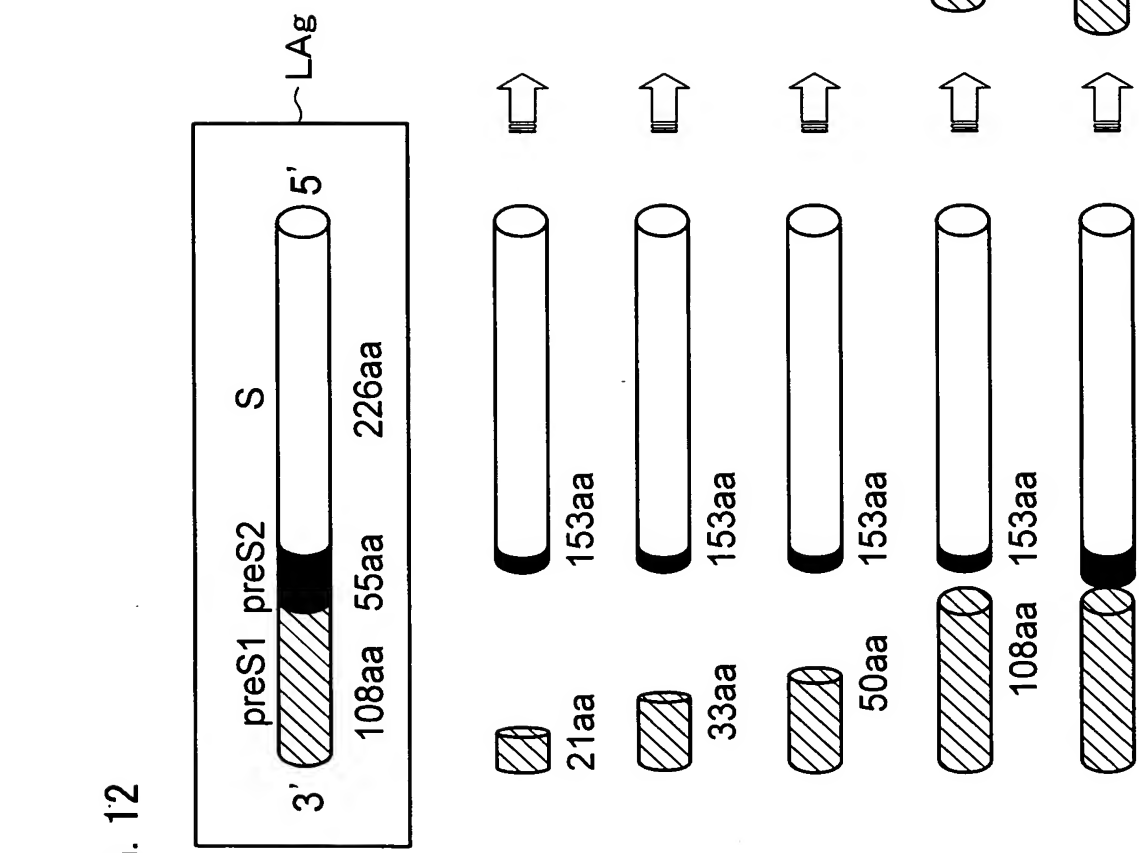

LAg
preS1 preS2 S
5'
3'
108aa 55aa 226aa
Not I
:Δ21-153
:Δ33-153
:Δ50-153
:Δ108-153
:Δ127-153
21aa
33aa
50aa
108aa
127aa
153aa

FIG. 13

Pyrobest POLYMERASE (TaKaRa)	DNA	0.5 μl
10×PCR BUFFER		5 μl
dNTP MIXTURE (10mM)		5 μl
TEMPLATE DNA(5 μg/ml)		2 μl
PRIMER (F)(100 μM)		1 μl
PRIMER (R)(100 μM)		1 μl
DISTILLED WATER		35.5 μl
TOTAL		50 μl

FIG. 14

	CYCLE	TEMPERATURE	TIME
1	1	98℃	30 sec.
2	30	98℃	30 sec.
		55℃	1 min.
		68℃	30 min.
3	1	4℃	∞

FIG. 15

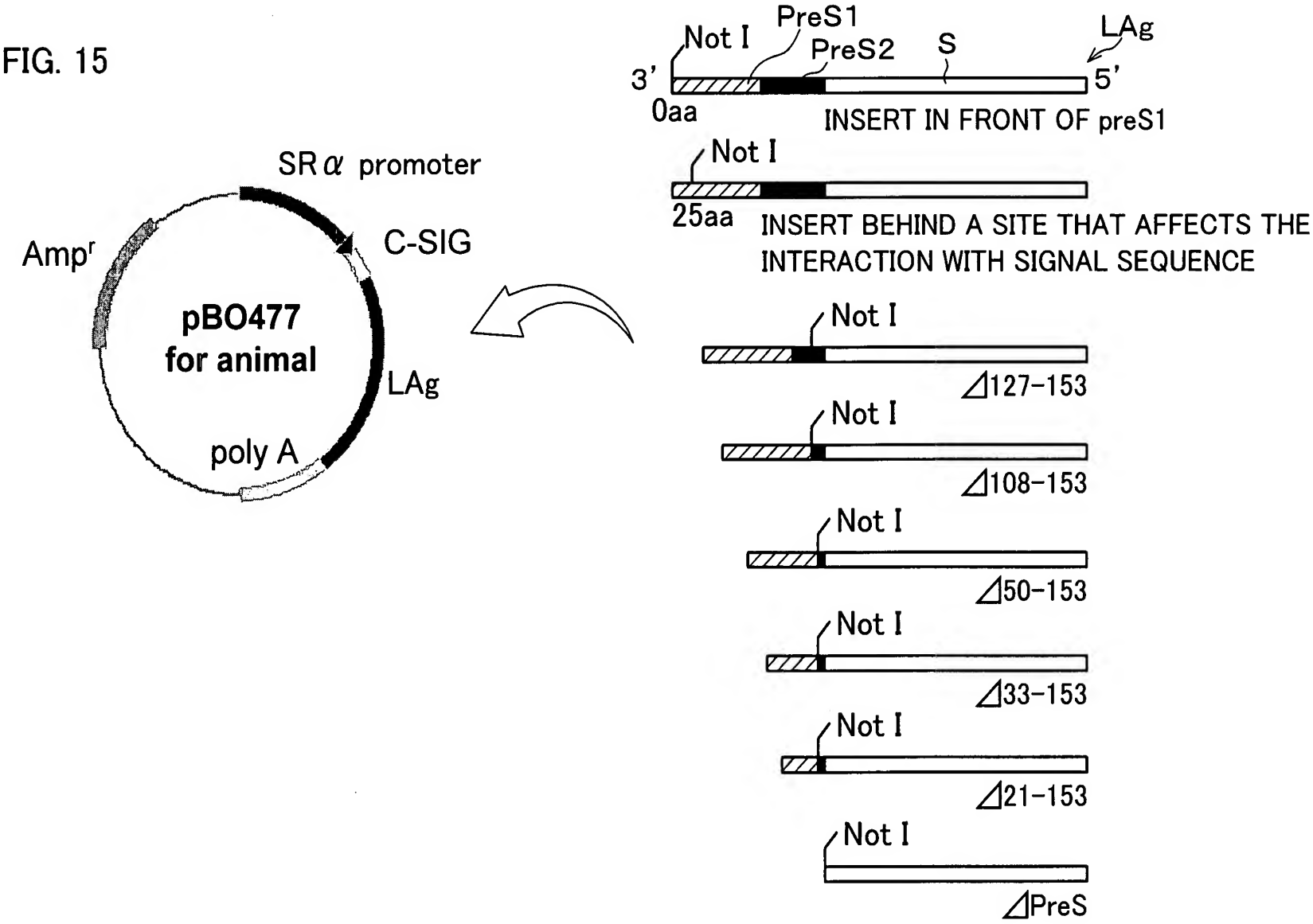


FIG. 16 (a) SUPERNATANT (×2 DILUTED)

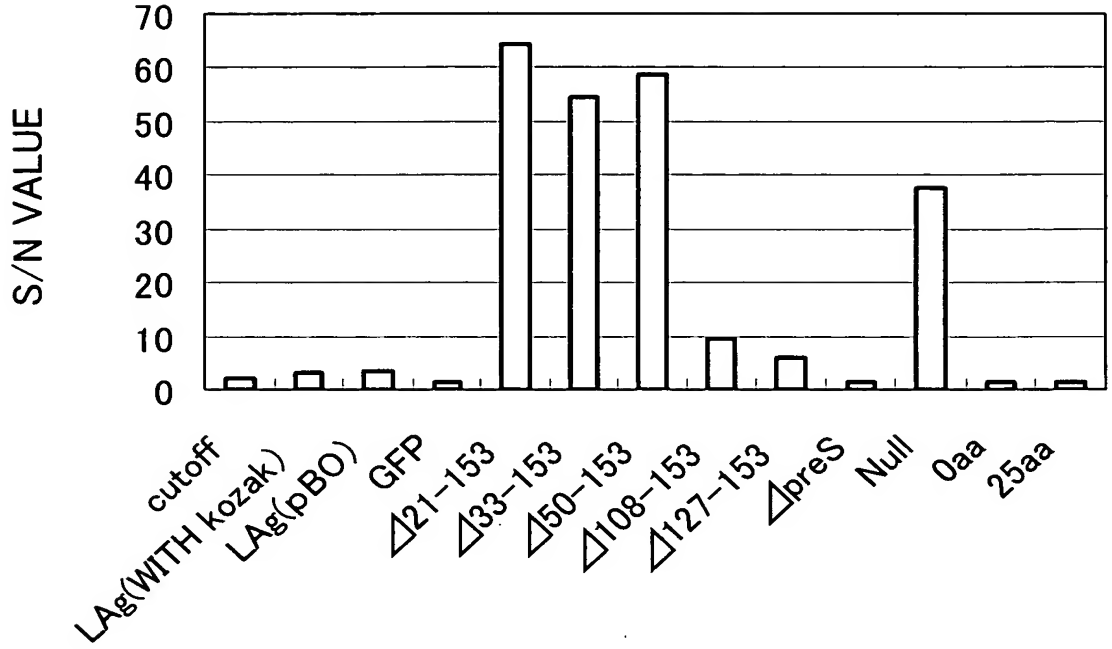


FIG. 16 (b) CELLS (×200 DILUTED)

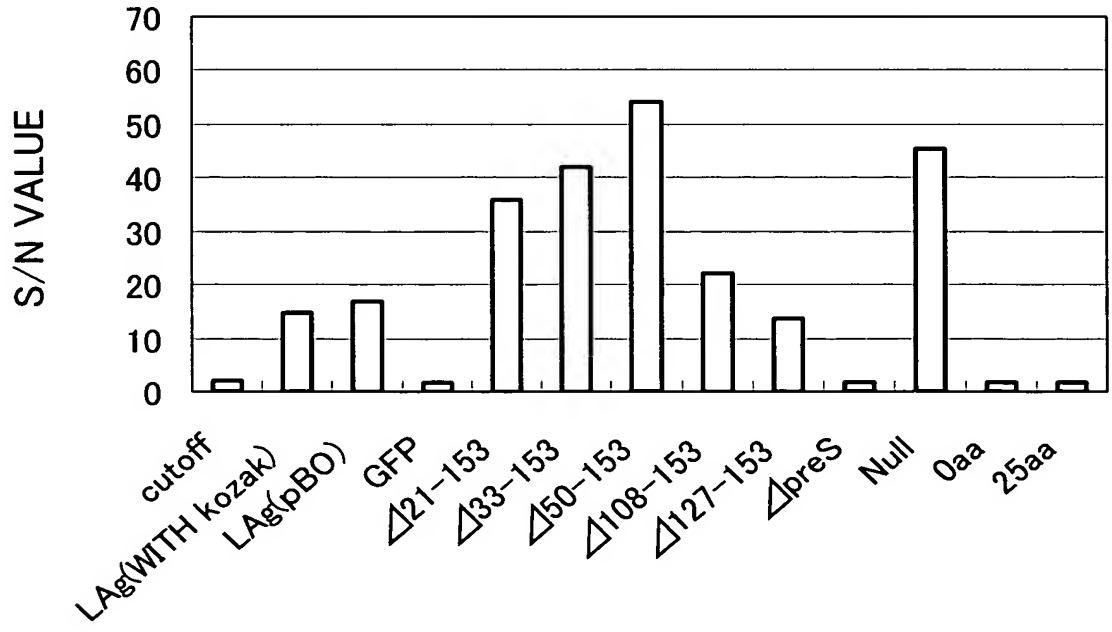


FIG. 17

	SUPERNATANT(×2 DILUTED)			CELLS (×200 DILUTED)		
plasmid	S/N	RATE	DECISION	S/N	RATE	DECISION
LAg(WITH kozak)	3.13	26.6	R	14.74	115.0	R
LAg(pBO)	3.68	31.3	R	17.00	132.6	R
GFP	1.41	12.0		1.69	13.2	
⊿21-153	64.54	548.6	R	35.79	279.2	R
⊿33-153	54.39	462.3	R	42.03	327.8	R
⊿50-153	58.67	498.7	R	54.19	422.7	R
⊿108-153	9.58	81.4	R	22.32	174.1	R
⊿127-153	5.93	50.4	R	13.73	107.1	R
⊿preS	1.52	12.9		1.59	12.4	
Null	37.73	320.7	R	45.41	354.2	R
0aa	1.42	12.1		1.65	12.9	
25aa	1.46	12.4		1.6	12.5	

FIG. 18

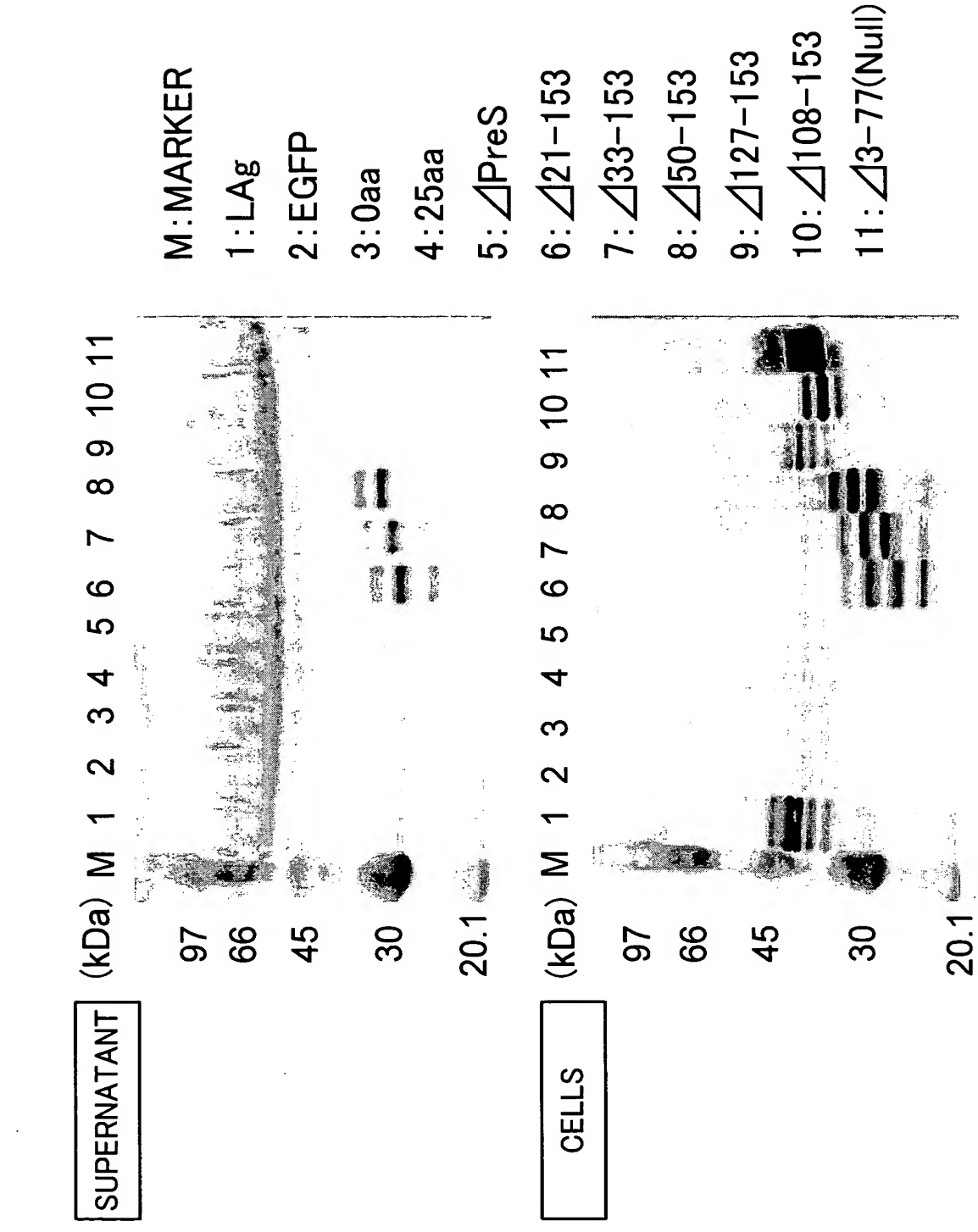

(a)
SUPERNATANT
(kDa) M 1 2 3 4 5 6 7 8 9 10 11
97
66
45
30
20.1
M:MARKER
1:LAg
2:EGFP
3:0aa
4:25aa
5:⊿PreS
6:⊿21-153
7:⊿33-153
8:⊿50-153
9:⊿127-153
10:⊿108-153
11:⊿3-77(Null)
(b)
CELLS
(kDa) M 1 2 3 4 5 6 7 8 9 10 11
97
66
45
30
20.1

FIG. 19

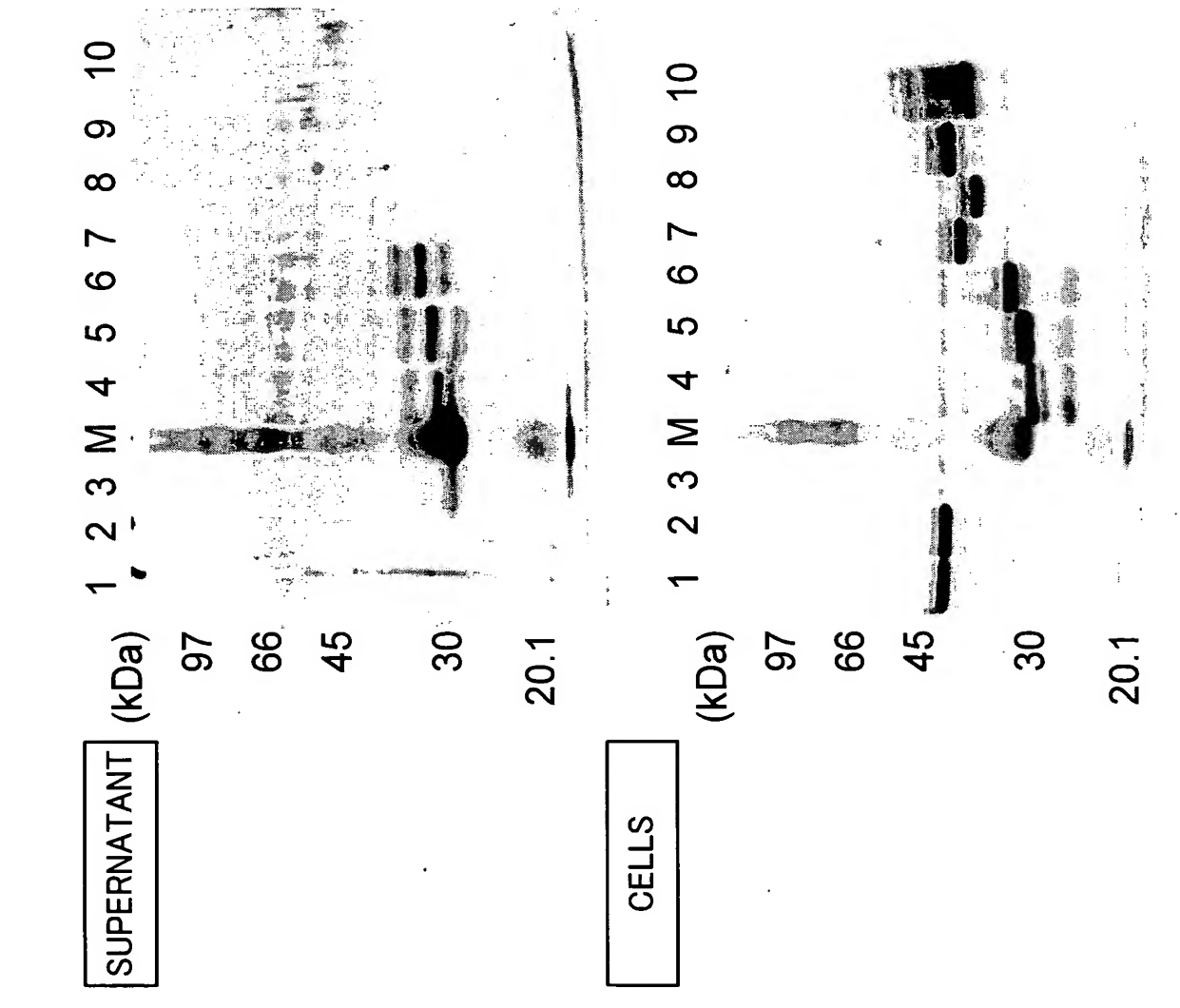

(a)
SUPERNATANT
(kDa)
97
66
45
30
20.1
1 2 3 M 4 5 6 7 8 9 10
M:MARKER
1:LAg(kozak)
2:LAg
42.9kDa
3:EGFP
4:Δ21-153
29.4kDa
5:Δ33-153
30.5kDa
6:Δ50-153
32.9kDa
7:Δ127-153
41.2kDa
8:Δ108-153
38.5kDa
9:Δ51-66
43.8kDa
10:Δ3-66(Null)
40.1kDa
(b)
CELLS
1 2 3 M 4 5 6 7 8 9 10
(kDa)
97
66
45
30
20.1

FIG. 20

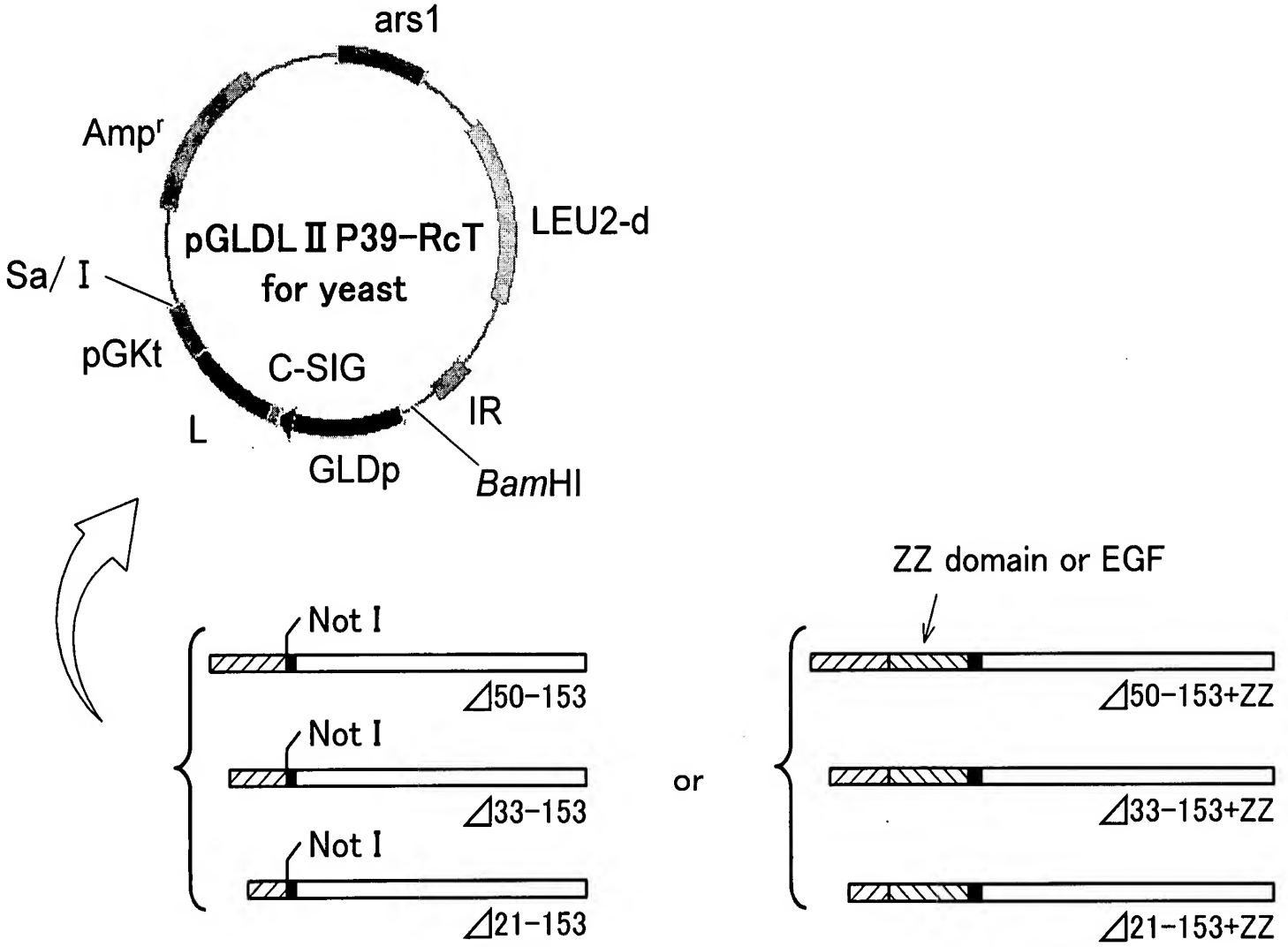


FIG. 21

STRAIN	S/N
LAg	233
⊿21-153	255.03
⊿33-153	189.22
⊿50-153	318.45
⊿21-153+ZZ	・・・
⊿33-153+ZZ	280.18
⊿50-153+ZZ	304

FIG. 22

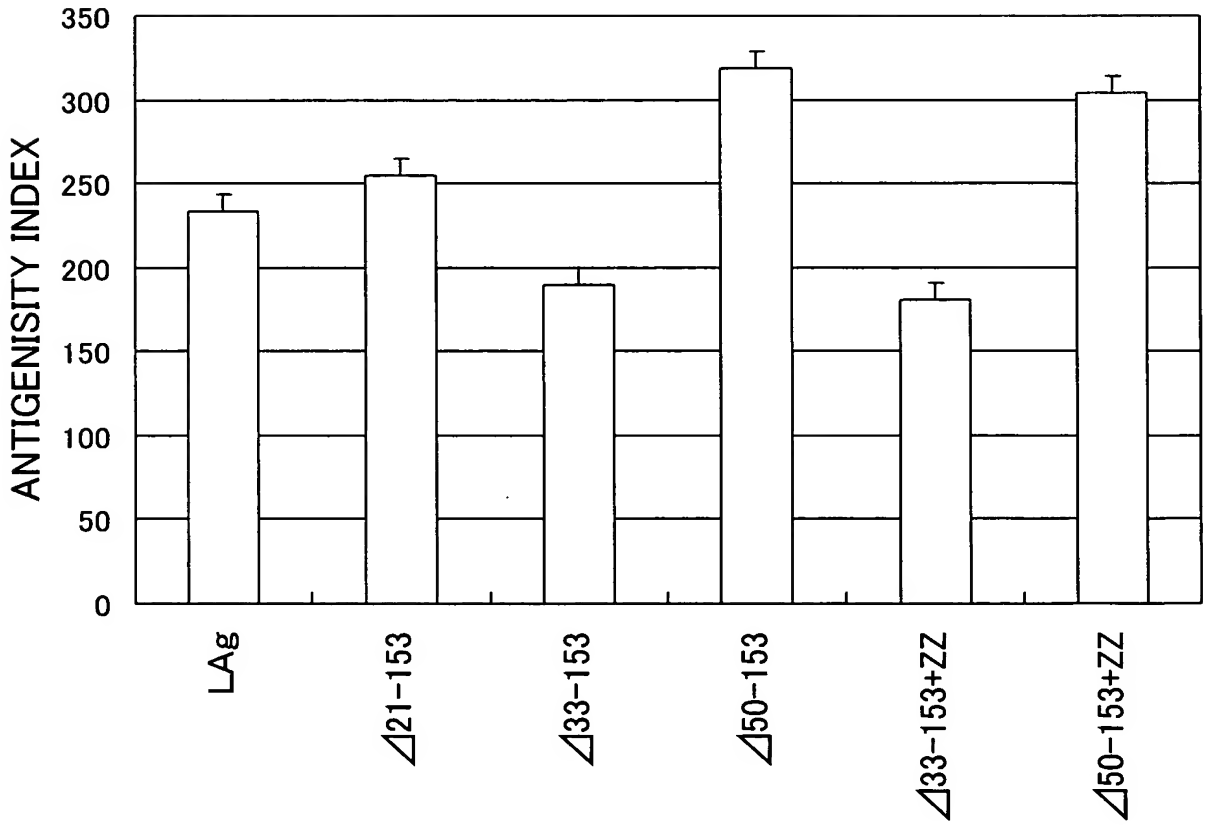


FIG. 23

PROTEINS ATTACKING CYTOPLASMIC RNA SUCH AS RNase	Pancreatic type Rnases from vertebrates
	RNase 1 or Bovine RNase A
	Eosinophil derived neurotoxin
	Eosinophil cationic protein
	Liver RNase (RNase 4)
	Angiogenin
	Bovine seminal RNase
	Frog Rnases (Onconase etc.)
PROTEINS OBSTRUCTING MEMBRANE TRANSPORT	Streptolysin(Streptococcus pyogenes)
	Cholesterol binding toxins (Streptococcus. Bacillus. Clostridium. Listeria)
	alpha-Toxin (Staphylococcus aureus)
	Delta-Toxin (Staphylococcus aureus) and melittin (Apis mellifera)
	Aerotysin (Aeromonas hydrophila)
	Escherichia coli hemolysin
PROTEINS OBSTRUCTING SIGNAL TRANSDUCTION	Cholera toxin (Vibrio cholerae)
	Heat-labile enterotoxins (Escherichia ColID
	Pertussis toxin (Bordetella periussis)
	Exoenzyme C3 (Clostridium botulinum)
	Adenylate cyclase toxin (Bordetella sp.)
	Anthrax edema factor (Bacillus anthracis)
PROTEINS OBSTRUCTING PROTEIN SYNTHESIS	Diphtheria toxin (Corynebacterium diphtheriae)
	Pseudomonas aeruginosa exotoxin A
	Shiga toxins (Shigella dysenteriae serotype I, Escherichia Coli)
	Ricin (Ricinus communis)
	Ribosome-inactivating proteins
	alpha-Sarcin and related toxins (Aspergillus)
PROTEINS DISTURBING CYTOSKELTON	C2 toxin (Clostridium botulinum type C and D)
	Cytotoxic necrotizing factors (Escherichia coli)
	Enterotoxin A and cytotoxin B (Clostridium difficile)
	ActA (Listeria monocytogenes)
	IcsA (Shigella flexneni)
	Zonula occludens toxin (Vibrio cholerae)

FIG. 24

PROTEINS SUPPRESSING IMMUNITY OR INFLAMMATORY REACTION	Pyrogenic exotoxins (superantigens) (Staphylococcus aureus and Streptococcus pyogenes)
	Anthrax lethal toxin (Bacillus anthracis)
	Leukocidins and gamma lysins (Staphylococcus sp.)
PROTEINS DISTURBING MEMBRANE TRANSPORT	Tetanus neurotoxin (Clostridium tetani)
	VAMP-specific botulinum neurotoxins
	Botulinum neurotoxins type A and E (Clostridium botulinum)
	Botulinum neurotoxin type C (Clostridium botulinum)
	Vacuolating cytotoxin (Helicobacter pylonD
Na CHANNEL DISTURBING PROTEINS	alpha-Scorpion toxins
	beta-Scorpion toxins
	Excitatory insect selective neurotoxins from scorpion venoms
	Depressant insect selective neurotoxins from scorpion venoms
	mu-Conotoxins (Conus geographus)
	mu-Agatoxins (Agelenopsis aperta)
	Anthopleurin-A. -B, and -C (anemone toxin)
	Anemone toxins (type II)
	Calitoxins
K CHANNEL DISTURNING PROTEINS	Kaliotoxin
	Scyllatoxin (Leiurus quinquestriatus hebraeus)
	Apamin (honey bee Apis mellifera)
	MCD peptide (honey bee Apis mellifera)
	Charybdotoxin and iberiotoxin (Leiurus quinquestriatus var. hebraeus and Buthus tamul us)
	Margatoxin, noxiustoxin, and kaliotoxin (Centruroides margaritatus. Centruroides noxius, Androctonus mauretanicus)
	Dendrotoxins (Dendroaspis species)
	Sea anemone potassium channel toxins

FIG. 25

Ca CHANNEL DISTURBING PROTEINS	Omega-Conotoxins (Conus spp.)
	Omega-Agatoxins (Agelenopsis aperta)
	Omega-Grammotoxin SIA (Grammostola spatulata Chilean pink tarantula)
	Hololena toxin (Hololena curta)
	PLTXII (Plectreurys tristes)
	Calciseptine (Dendroaspis polylepis)
	Calcicludine (Dendroaspis angusticeps)
	beta-Leptinotarsin-h
	Taicatoxin (Oxyuranus scutelatus scutelatus)
ACETYLCHOLINE RECEPTOR DISTURBING PROTEINS	alpha-Bungarotoxin (Bungarus multicinctus)
	alpha-Cobratoxin (Naja kaouthia)
	Erabutoxins (Laticauda semifasciata)
	Toxin alpha ('Naja nigricollis')
	kappa-Bungarotoxin (Bungarus multicinctus)
	alpha-Conotoxins (Conus spp.)
	Snake toxins against muscarinic acetylcholine receptors
	Muscarinic toxin-1~-5, -7, m1-toxin from green mamba (Dendroapsis angusticeps)
	Muscarinic toxin-alpha, -beta from black mamaba (Dendroapsis polylepis)
RYANODINE RECEPTOR Ca^{2+} CHANNEL DISTURBING PROTEINS	Helothermine (Heloderma horridum horridum)

FIG. 26

PRESYNAPTIC DISTURBING PROTEINS	PRESYNAPTIC DISTURBING PROTEINS
	Rattlesnake venom neurotoxins: crotoxin-related proteins
	Ammodytoxins (Vipera ammodytes ammodytes)
	Notexins (Notechis scutatus scutatus)
	Textilotoxin (Pseudonaja textilis textilis)
	Tai poxin
	alpha-Latrotoxin (black widow spider)
	alpha-Latroinsectotoxin (Latrodectus mactans tred ecimguttatus)
	Pardaxin (Pardachirus marmoratus)
	Palytoxin (Corals of the spp. Palythoa)
	Equinatoxins (Actinia equina L., sea anemone)
GLUTAMIC ACID RECEPTOR DISTURBING PROTEINS	Conantokins (Conus spp.)

FIG. 27

		TIME AFTER GCV ADMINISTRATION (DAYS)						
		0	1	3	6	9	12	15
TUMOR SIZE (%)	A431	100	102	97	94	85	72	66
	WiDr	100	105	107	111	118	125	133